3-Bromo-6-nitro-1-phenyl-1*H*-indazole (7b): long yellow needles; mp 172–172.5 °C (ethanol–chloroform 10:1). Anal. Calcd for $C_{13}H_8BrN_3O_2$: C, 49.09; H, 2.55; N, 13.21. Found: C, 48.98; H, 2.75; N, 13.07. IR 1345 and 1500 cm^{-1} (C–NO_2); ^1H NMR (300 MHz, Me_2SO-d_6) δ 8.55 [s, 1, H-7], 8.15 [d, 1, $J_{4,5}$ = 10 Hz, H-5], 7.98 [d, 1, H-4], 7.81–7.84 [d, 2, $J_{2'3'}$ = 8 Hz, H-2'], 7.65–7.68 [t, 2, $J_{3'4'}$ = 8 Hz, H-3'], 7.54–7.57 [t, 1, H-4'].

3,5-Dinitro-1-phenyl-1*H*-indazole (8a): yellow crystals; mp 152–152.5 °C (ether–acetone 1:1); high-resolution mass spectrum, calcd for $C_{13}H_8N_4O_4$ 284.0545; found 284.0551; IR 1350 and 1520 cm^{-1} (C–NO_2); ^1H NMR (100 MHz, Me_2SO-d_6) δ 9.44 [d, 1, $J_{4,6}$ = 4 Hz, H-4], 8.57 [dd, 1, $J_{6,7}$ = 10 Hz, H-6], 7.98 [d, 1, H-7], 7.64–7.90 [m, 5, H phenyl].

6-Nitro-1-phenyl-1*H*-indazole (11):[19] ^1H NMR (300 MHz, $CDCl_3$) δ 8.61 [m, 1, $J_{5,7}$ = 1.8 Hz, $J_{4,7}$ = 0.5 Hz, $J_{3,7}$ = 0.9 Hz, H-7], 8.31 [d, 1, H-3], 8.07 [dd, 1, $J_{4,5}$ = 8.8 Hz, H-5], 7.90 [dd, 1, H-4], 7.67–7.71 [d (broad), 2, $J_{2'3'}$ = 7.5 Hz, H-2'], 7.56–7.61 [t (broad), 2, $J_{3'4'}$ = 7.5 Hz, H-3'], 7.42–7.47 [tt, 1, $J_{2'4'}$ = 1.2 Hz, H-4'].

3,6-Dinitro-1-phenyl-1*H*-indazole (8b): light yellow crystals; mp 192–193.5 °C (ether–acetone 1:1); high-resolution mass spectrum, calcd for $C_{13}H_8N_4O_4$ 284.0545, found 284.0542; IR 1515 and 1335 cm^{-1} (C–NO_2); ^1H NMR (300 MHz, Me_2SO-d_6) δ 8.63 [d, 1, $J_{5,7}$ = 1.9 Hz, H-7], 8.5 [d, 1, $J_{4,5}$ = 8.7 Hz, H-4], 8.41 [dd, 1, H-5], 7.91–7.95 [d (broad) 2, $J_{2'3'}$ = 8 Hz, H-2'], 7.37–7.78 [t (broad), 2, $J_{3'4'}$ = 8 Hz, H-3'], 7.65–7.70 [t (broad), 1, H-4'].

Acknowledgment. We are grateful to B. van Vliet for help with the GLC analyses, to Drs. C. Erkelens for the NMR spectra and to Dr. J. van Thuijl and J. J. van Houte for the mass spectral analyses. We also thank Drs. H. A. Dingjan of the Department of Analytical Chemistry in the School of Pharmacy for help and information concerning the detection of NO_2 and bromine.

Appendix

Attempt to Synthesize 7b. No bromination products were obtained, i.e., neither bromination occurs in the phenyl ring nor in the 3 or any other position in the indazole nucleus when 11 was subjected to the following bromination reactions: Br_2 in refluxing acetic acid for 1–24 h; dioxane and Br_2 in ether solution; dioxane and Br_2 in dioxane solution; Br_2–$FeBr_3$ in carbon tetrachloride. Only unreacted 11 was recovered.

Registry No. **2a**, 91178-53-9; **2b**, 91178-54-0; **5a**, 83553-83-7; **5b**, 83553-84-8; **6a**, 67400-25-3; **6b**, 70315-68-3; **7a**, 91178-55-1; **7b**, 91178-56-2; **8a**, 91178-57-3; **8b**, 91178-58-4; **10**, 3682-71-1; **11**, 91178-59-5; C_6H_5Br, 108-86-1; $C_6H_5CH_2Br$, 100-39-0; NO_2, 10102-44-0; Br_2, 7726-95-6.

Generation of Azomethine Ylides via the Desilylation Reaction of Immonium Salts

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Generation of intermediates having azomethine ylide reactivity was achieved by the reaction of several ethanol or thioimidate derivatives with methyl iodide followed by treatment of the resulting imine with (trimethylsilyl)methyl triflate. Desilylation of the resulting salt with cesium fluoride generates an azomethine ylide which undergoes a subsequent 1,3-dipolar cycloaddition reaction with added dipolarophiles. The cycloadduct formed when dimethyl acetylenedicarboxylate is used as the dipolarophile undergoes loss of ethanol or methyl mercaptan to give *N*-methyl-2-phenyl-3,4-dicarbomethoxypyrrole. Reaction of the analogous thioimidate ylide with acetylene dipolarophiles also proceeds smoothly and affords related cycloadducts. The cesium fluoride induced desilylation reaction shows all the characteristics of a concerted cycloaddition, including stereospecificity when dimethyl fumarate and maleate are used as the dipolarophiles.

The 1,3-dipolar cycloaddition reaction represents one of the best methods for the synthesis of five-membered heterocyclic ring systems.[1,2] The ease of the cycloaddition, the rapid accumulation of polyfunctionality in a relatively small molecular framework, the high stereochemical control of the cycloaddition, and the fair predictability of its regiochemistry have contributed to the popularity of the reaction in organic synthesis.[3,4] In the realm of alkaloid synthesis, in which a premium is put on the rapidity of construction of polyfunctional, highly bridged carbon and heteroatom networks, the dipolar cycloaddition reaction has now emerged as a prominent synthetic method.[5] Most of the studies to date have hinged upon the use of nitrones,[6-11] nitrile oxides,[12-16] and azomethine imines.[17] Fewer accounts have been concerned with azomethine

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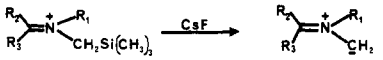
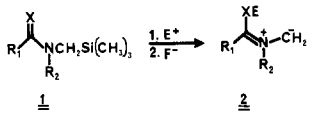
ylides.[18-20] The pyrrolidine ring is a frequently encountered structural unit of many synthetically challenging alkaloids.[21] One of the most conceptually simple ways of pyrrolidine formation is 1,3-dipolar cycloaddition of an azomethine ylide with an olefin. Although ring opening of aziridines to azomethine ylides works well when the substituent groups are capable of stabilizing the dipole centers,[22-28] the ring cleavage fails completely when simple alkyl substituents are used. An alternate route to nons-



tabilized azomethine ylides was recently developed by Vedejs and involves desilylation of an appropriately substituted immonium cation.[29-33] The fluoride-induced desilylation has become a useful tool for the generation of nucleophilic carbon species.[34] The research described herein was aimed at demonstrating the usefulness of amides and vinylogous amides as azomethine ylide equivalents.[35]

Results and Discussion

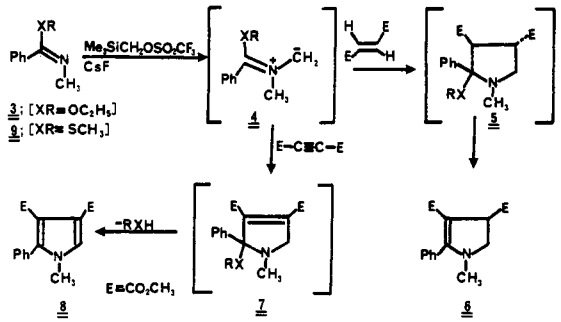
The propensity of silicon to transfer to a silylophile when bound to an electronegative carbon raised the possibility of desilylation of an intermediate such as **1** as a method



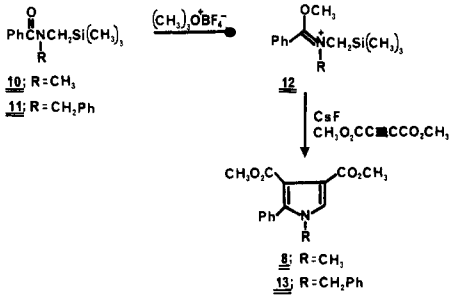
for generating azomethine ylides. With the hope that such a dipolar species would be formed and participate in a cycloaddition, we investigated the cesium fluoride induced desilylation reaction of several immonium salts derived from amides, thioamides, and vinylogous amides.

As our first model we chose to investigate the cycloaddition reaction of several imidate and thioimidate ylides with a number of different dipolarophiles. Alkylation of imidate **3** with (trimethylsilyl)methyl triflate followed by cesium fluoride desilylation of the resulting salt afforded azomethine ylide **4**. Cycloaddition of this transient species with dimethyl fumarate produced dihydropyrrole **6**. The initially formed cycloadduct **5** readily loses a molecule of ethanol under the reaction conditions to give **6**. Similarly, treatment of **3** with $Me_3SiCH_2OSO_2CF_3$, CsF, and dimethyl acetylenedicarboxylate produced pyrrole **8** in 48% yield.

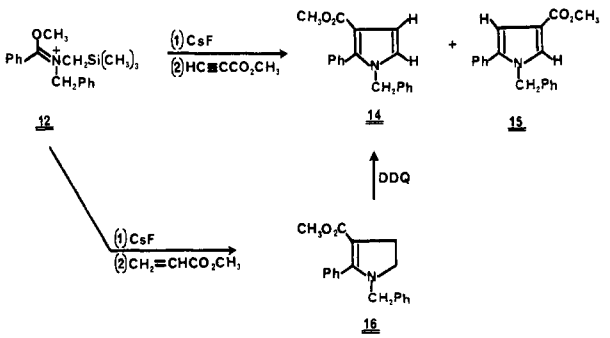
An alternative route to **8** begins with N-alkylation of thioimidate **9** with $Me_3SiCH_2OSO_2CF_3$. The crude salt



is stirred with dimethyl acetylenedicarboxylate and anhydrous cesium fluoride to effect 1,3-dipolar cycloaddition. Loss of methyl mercaptan from the initially formed cycloadduct **7** afforded pyrrole **8** in 74% yield. The higher yield of pyrrole **8** obtained from the thioimidate ylide is probably related to the facility of thioamide alkylation as well as the greater stability of the thioimidate salt.[36] All attempts to obtain a cycloadduct from the reaction of ylide **4** with nonactivated olefins (i.e., cyclohexene, 1-octene, norbornene, etc.) failed. It should also be noted that pyrrole **8** (or **13**) could be obtained in good yield by the sequential treatment of benzoyl amide **10** (or **11**) with Meerwein's reagent followed by desilylation with cesium fluoride in the presence of dimethyl acetylenedicarboxylate.



The reaction of iminium salt **12** (R = CH_2Ph) with an unsymmetrically substituted dipolarophile such as methyl propiolate was also studied and was found to produce a mixture of two pyrroles (**14**:**15** = 2:1). The crude residue was chromatographically separated and each regioisomer could be obtained in pure form. The NMR spectrum of the 2,3-disubstituted pyrrole **14** exhibits an AB quartet at



δ 6.82 (J = 3.2 Hz) with a typical ortho coupling constant

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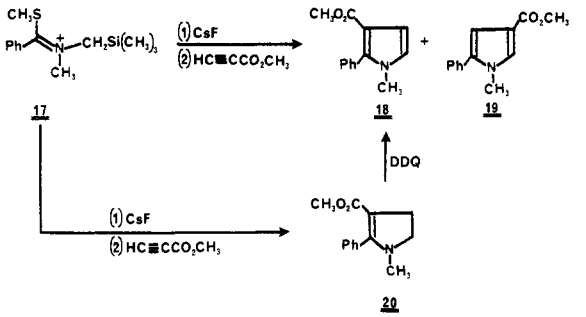
(35) A preliminary account of this work has been presented, see: Padwa, A.; Haffmanns, G.; Tomas, M. *Tetrahedron Lett.* **1983**, *24*, 4303.
(36) Similar observations have been made by Vedejs and West. We thank Professor Vedejs for informing us of his method of generating thioimidate methylides from *N*-[(trimethylsilyl)methyl]thioamides by a sequence involving S-alkylation with methyl triflate followed by desilylation with cesium fluoride: Vedejs, E.; West, F. G. *J. Org. Chem.* **1983**, *48*, 4773.

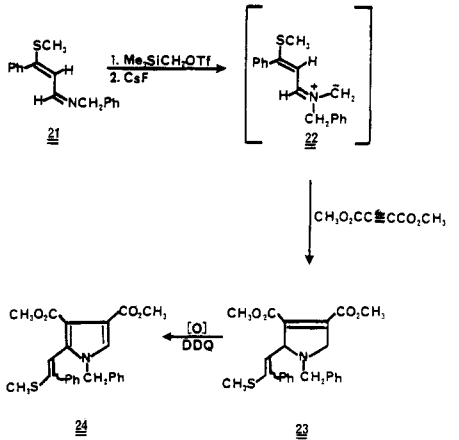
for the pyrrole ring.[37] The doublet pattern of the pyrrole protons of the 2,4-isomer (**15**) (J = 1.9 Hz) is quite normal as it has been shown that the cross-ring or meta coupling constant in the pyrrole system has a value of approximately 2.0 Hz.[37] Surprisingly, the reaction of the azomethine ylide derived from **12** with methyl acrylate produced a single cycloadduct whose structure was established as dihydropyrrole **16** on the basis of its spectral data (see Experimental Section) and by its DDQ oxidation to pyrrole **14**.

Cycloaddition of the dipole derived from thioimidate **17** with methyl propiolate was found to produce a 1:1 mixture of pyrroles **18** and **19**. Cycloaddition with methyl acrylate,



on the other hand, was in accord with the earlier observations and produced a single regioisomer. The labile cycloadduct **20** was not isolated in pure form but rather was oxidized with DDQ to the corresponding 2,3-disubstituted pyrrole **18**. A much higher yield of the pyrrole system was obtained with the thioimidate ylide as compared with its oxygen analogue. Vedejs and West made similar observations and also found that the regiochemistry of cycloaddition with methyl propiolate is not as clean as that encountered with methyl acrylate.[36]

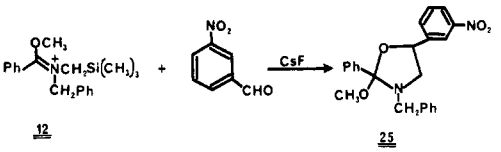
Generation of intermediates having azomethine ylide reactivity was also achieved by the reaction of vinylogous amides or thioamides with methyl iodide followed by treatment of the resulting imine with $Me_3SiCH_2OSO_2CF_3$, cesium fluoride, and an appropriate trapping reagent. Azomethine ylide **22** undergoes cycloaddition with di-



methyl acetylenedicarboxylate to give **23** even though **22** could undergo a 1,5-electrocyclization reaction.[38,39] Structure **23** was further established by its oxidation to pyrrole **24** on heating with DDQ in benzene.

The parent azomethine ylide system is predicted to react readily with both electron-deficient and electron-rich dipolarophiles due to the narrow frontier orbital separation.[40] Substituent groups on the dipole should be capable of changing the azomethine ylide to a LU-controlled system. According to FMO theory,[41] regioselectivity is the result of best overlap of the interacting orbitals, i.e., the atoms with the largest orbital coefficients combine preferentially. The dipole LU–dipolarophile HO interaction with the azomethine ylides derived from iminium salts **12** and **17** and methyl acrylate favors formation of the 2,3-disubstituted isomer (i.e., **16** and/or **20**). We suggest that the loss of regioselectivity with the propiolate cycloaddition results from the lower HO orbital energy of the propiolate (IP = 11.15 eV)[42] than that of the acrylate (IP = 10.72 eV).[43] Thus, interaction of the dipole HO orbital with the dipolarophile LU orbital will be of greater importance with methyl propiolate, thereby leading to a mixture of regioisomers.

Since the difference in regioselectivity with the propiolate as compared to the acrylate system was attributed to the lower orbital energy of the former, a similar effect would be anticipated when a more electron-deficient dipolarophile is used. We found that the reaction of the azomethine ylide derived from **12** with *m*-nitrobenzaldehyde afforded cycloadduct **25** as the exclusive product.



A distinction between the two possible regioisomers was made on the basis of the chemical shift of the hydrogens in the NMR spectrum as well as the coupling constants (see Experimental Section). Other examples of the 1,3-dipolar cycloaddition reaction of azomethine ylides with carbonyl compounds are known in the literature and provide good analogy for the formation of cycloadduct **25**.[44,45] The exclusive formation of **25** is the result of the union of the larger azomethine ylide HO coefficient on the unsubstituted carbon with that of the larger dipolarophile LU coefficient on the carbon atom of the carbonyl group.

Treatment of 3-(benzylamino)cyclohexenone (**26**) with methyl iodide followed by reaction with (trimethylsilyl)methyl triflate gave immonium salt **28** in good yield. The crude salt was dissolved in dimethoxyethane and was stirred with methyl propiolate and anhydrous cesium fluoride to effect the 1,3-dipolar cycloaddition. After the reaction had stirred for 3 h, a 70% yield of cycloadduct **29** could be isolated. When methyl acrylate was used as the dipolarophile, cycloadduct **30** was formed in 85% yield. Hydrolysis of the enol ether afforded lactam **32** as the exclusive product. Structure **32** was independently synthesized by treating 3-ethoxycyclohexenone with the anion derived from *N*-benzyl γ-lactam. The conversion of **30** to **32** probably involves the initial formation of a ring-opened intermediate (i.e., **31**) which subsequently cyclizes under the reaction conditions. Through this series of reactions, enamide **26** was converted into **32** in 75% overall yield (Scheme I). The formation of a single regioisomer (i.e., **29** or **30**) from the above cycloaddition is consistent with

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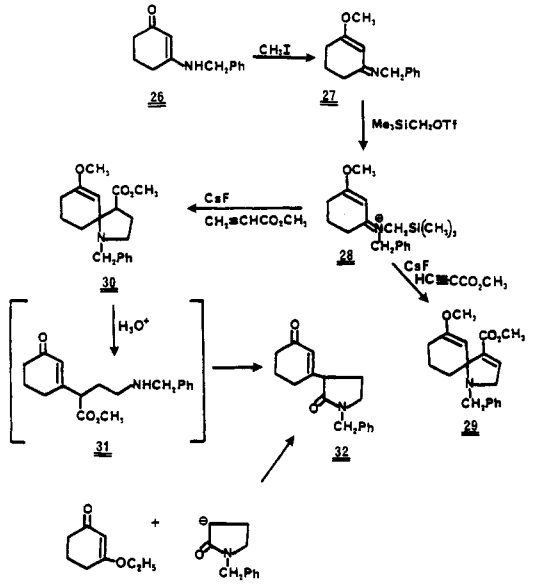
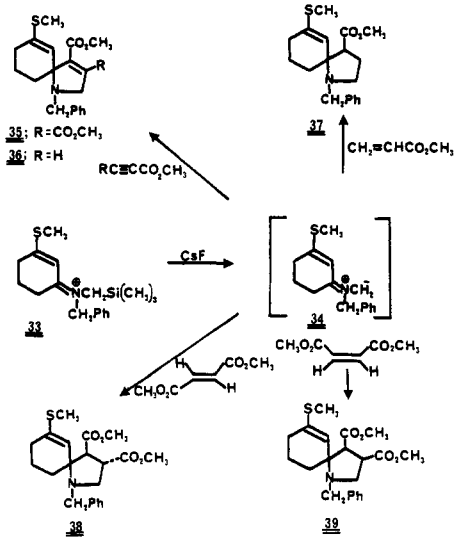
Scheme I



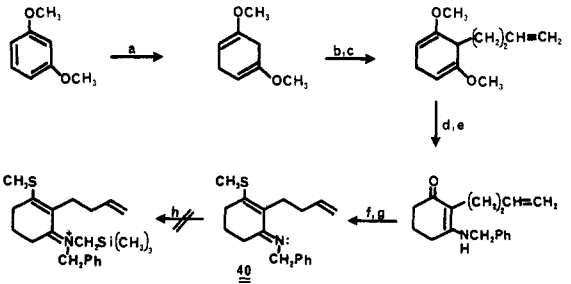
frontier MO theory.[41] When azomethine ylides are used as 1,3-dipoles, the dipole highest occupied (HOMO) and dipolarophile lowest unoccupied (LUMO) interaction will be of greatest importance in stabilizing the transition state. Both conjugating and electron-attracting groups accelerate reactions of dipolarophiles with azomethine ylides as compared to ethylene. The preferential formation of cycloadduct **29** (or **30**) is the result of the union of the larger azomethine ylide HO coefficient on the methylene carbon with that of the larger dipolarophile LU coefficient on the unsubstituted carbon.

Reaction of the analogous thioimidate ylide **34** with acetylenic dipolarophiles also proceeds smoothly and affords related cycloadducts. Using dimethyl acetylenedicarboxylate as the dipolarophile, the corresponding thioether adduct **35** can be isolated in 80% yield. With methyl



propiolate, the cycloaddition reaction proceeds with complete regioselectivity to give adduct **36** in 70% yield. Similarly, treatment of **33** with cesium fluoride in the presence of methyl acrylate provided cycloadduct **37** in good yield. All octet-stabilized 1,3-dipoles examined so far in the literature have been shown to undergo stereospecific cis cycloaddition.[1,2] In order to determine whether the azomethine ylide generated from the desilylation of **33** behaves similarly, we studied the cycloaddition with cis- and trans-disubstituted dipolarophiles. The reaction

Scheme II[a]

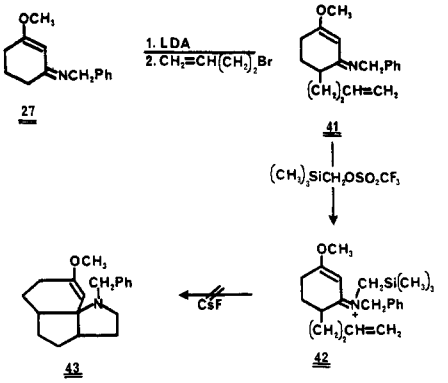


[a] Reagents: (a) Na, NH_3 (ethanol); (b) *t*-BuLi; (c) $Br(CH_2)_2CH{=}CH_2$; (d) HCl/H_2O; (e) NH_2CH_2Ph, Δ; (f) Lawesson's reagent; (g) CH_3I; (h) $(CH_3)_3SiCH_2OTf$.

proceeded with complete stereospecificity with dimethyl fumarate and maleate giving rise to cycloadducts **38** (mixture of diastereomers (87%)) and **39** (75%). The above cycloadditions show all the characteristics of a concerted reaction, including stereospecificity and regioselectivity and therefore, are consistent with the intermediacy of an azomethine ylide (i.e., **34**).

Intramolecular dipolar cycloadditions have much synthetic potential.[46] To apply the above methodology in this context we first investigated the cycloaddition behavior of the thioimidate ylide derived from imine **40**. The synthesis of this compound is outlined in Scheme II. Unfortunately, all attempts to alkylate **40** with (trimethylsilyl)methyl triflate were unsuccessful, probably as a result of steric factors, and further work with this system was abandoned.

In order to circumvent the alkylation problem, we used imine **41** as our starting material. This compound was obtained in good yield by treating the anion derived from **27** with 4-bromo-1-butene. Reaction of **41** with (trimethylsilyl)methyl triflate followed by treatment of the resulting salt **42** with cesium fluoride resulted in the for-

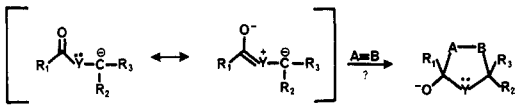


mation of a complex mixture of products which resisted all attempts at purification. Similar results were obtained when other standard desilylating reagents were used. In all of these cases no signs of an internal cycloadduct (i.e., **43**) were evident in the crude reaction mixture (NMR analysis). The negative results encountered with **42** are probably the result of a large frontier orbital gap which exists between the transient azomethine ylide and the neighboring olefinic double bond. It would seem as though the favorable entropy of reaction is not sufficient to overcome the unfavorable electronic factors. It should be noted that bimolecular reactions of azomethine ylides with alkyl-substituted alkenes have never been observed,

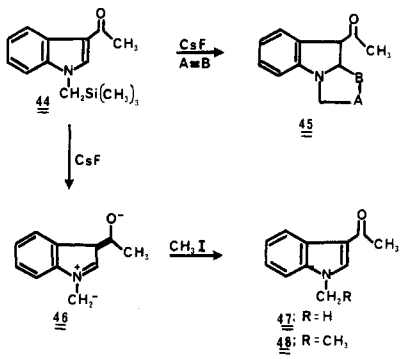
(46) For some leading references see: Padwa, A.; Rodriguez, A.; Tohidi, M.; Fukunaga, T. *J. Am. Chem. Soc.* **1983**, *105*, 933.

thereby indicating that the frontier orbital interaction is never large.

The hypothesis that a carbonyl group bonded to a heteroatom can provide dipole stabilization for formation of a carbanion adjacent to the heteroatom has been supported for esters, thio esters, and amides by experiment and theory.[47] Complexation of the counterion (i.e., lithium) to the carbonyl oxygen is clearly an important factor in the stabilization of these carbanions. Ab initio SCF calculations have suggested that dipole stabilization of carbanions can be of substantial magnitude even without counterion chelation.[48] As part of our work in this area

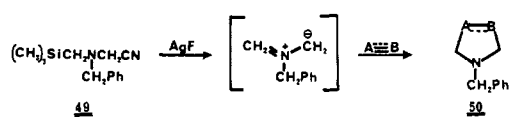


we became interested in determining whether dipole-stabilized carbanions which are devoid of counterion complexation could undergo 1,3-dipolar cycloaddition with added dipolarophiles. This led us to investigate the chemistry of *N*-[(trimethylsilyl)methyl]-3-acetylindole (**44**)

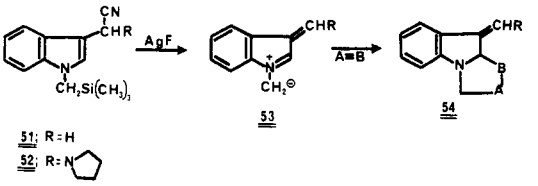


Our hope was to effect a desilylation reaction with cesium fluoride in the presence of a reactive dipolarophile so as to generate cycloadducts of type **45**. Numerous efforts to intercept azomethine ylide **46** using a variety of dipolarophiles failed. However, reaction of **44** with cesium fluoride in the presence of excess methyl iodide produced a 1:2 mixture of *N*-methyl **47** and *N*-ethyl-3-acetylindole (**48**). The ready desilylation of silane **44** with fluoride ion is undoubtedly related to the fact that the anion formed is favorably stabilized by the adjacent dipole (i.e., structure **46**). The α-amino carbanion undergoes alkylation with methyl iodide to give **48** or is protonated by the solvent to give **47**.

Since it was not possible to trap the dipole-stabilized carbanion **46** with added dipolarophiles, we decided to try an alternate approach. Recent work in our laboratory has shown that *N*-benzyl α-cyano amino silane **49** can act as



an azomethine ylide equivalent when treated with silver fluoride in the presence of electron-deficient olefins.[32] We hoped that an analogous process would also occur with the silyl cyano substituted indoles **51** and **52**. These compounds were readily prepared (see Experimental Section), but unfortunately, all attempts to trap the expected dipole **53** were unsuccessful.



In summary, the cesium fluoride induced desilylation reaction of immonium salts derived from amides, thioamides, and vinylogous amides provides access to reactive azomethine ylides in synthetically useful yields. Cycloaddition of the dipole-stabilized carbanion derived from the indole skeleton, on the other hand, does not occur. This is presumably a result of disruption of the indole aromaticity. The above method allows access to nonstabilized azomethine ylides and is currently being used in our laboratory to synthesize a number of alkaloids possessing the pyrroline ring.

Experimental Section[49]

Preparation of Dimethyl *N*-Methyl-2-phenyl-4,5-dihydropyrrole-3,4-dicarboxylate (6). A mixture containing 0.43 g of *N*-methyl benzenecarboximidic acid ethyl ester (**3**) in 15 mL of dimethoxyethane was treated with 0.79 g of (trimethylsilyl)methyl trifluoromethanesulfonate and subsequently with 0.5 g of cesium fluoride and 0.48 g of dimethyl fumarate for 10 h to give 0.4 g (42%) of dimethyl *N*-methyl-2-phenyl-4,5-dihydropyrrole-3,4-dicarboxylate (**6**): mp 93–94 °C; IR (KBr) 3000, 2850, 1720, 1680, 1610, 1600, 1560, 1500, 1440, 1420, 1340, 1330, 1280, 1190, 1140, 1060, 1040, 970, 920, 860, 770, and 720 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.51 (s, 3 H), 3.32 (s, 3 H), 3.50 (dd, 1 H, J = 10.0 and 2.0 Hz), 3.69 (s, 3 H), 3.86 (dd, 1 H, J = 8.0 and 2.0 Hz), 4.91 (dd, 1 H, J = 10.0 and 8.0 Hz), and 7.32 (s, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 34.95, 45.84, 49.99, 51.94, 57.05, 98.19, 127.82, 128.39, 128.88, 131.15, 164.08, 165.41, and 174.85; m/e 275 (M^+), 217, 216, 184 (base), 157, 130, 115, and 77; UV (methanol) 307 nm (ϵ 13 400).

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.39; H, 6.23; N, 5.06.

The structure of **6** was further verified by its oxidation to pyrrole **8** which was compared with an authentic sample.[50] A sample containing 150 mg of **6** and 200 mg of DDQ was stirred at 25 °C in 30 mL of benzene for 5 h. The black reaction mixture was washed with sodium carbonate and water, extracted with chloroform, and dried over magnesium sulfate to give 120 mg (81%) of **8** after removal of the solvent under reduced pressure.

Preparation of Dimethyl *N*-Methyl-2-phenylpyrrole-3,4-dicarboxylate (8). To a sample containing 0.45 g of *N*-methylbenzamide in 20 mL of anhydrous methylene chloride was added 0.63 g of triethyloxonium tetrafluoroborate. After stirring at 25 °C for 12 h, the reaction mixture was treated with 10 mL of a 10% sodium hydroxide solution. The organic layer was separated and dried over magnesium sulfate. Removal of the solvent left 434 mg (81%) of a yellow oil whose structure was assigned as *N*-methylbenzenecarboximidic acid ethyl ester (**3**). This material was dissolved in 20 mL of 1,2-dimethoxyethane and 0.79 g of (trimethylsilyl)methyl trifluoromethanesulfonate[51] was added. The solution was allowed to stir for 4 h and then 0.47 g of dimethyl acetylenedicarboxylate and 0.5 g of cesium fluoride were added to the mixture. After stirring for 12 h at 25 °C, the reaction mixture was washed with sodium bicarbonate solution.

(47) For a review, see: Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 725.
(48) Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J.; Chandrasekhar, J.; Schleyer, P. V. R. *J. Org. Chem.* **1981**, *46*, 4108.

(49) All melting points and boiling points are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, GA. The infrared absorption spectra were determined on a Perkin-Elmer 467 infrared spectrophotometer. The ultraviolet absorption spectra were measured with a Cary Model 14 recording spectrophotometer with 1-cm matched cells. The proton magnetic resonance spectra were determined at 90 MHz with a Varian EM-390 spectrometer. Mass spectra were determined with a Finnegan 4000 mass spectrometer at an ionizing voltage of 70 eV.
(50) Potts, K. T.; Roy, D. N. *Chem. Commun.* **1968**, 1061.
(51) Ambasht, S.; Chin, S. K.; Peterson, P. E.; Queen, J. *Synthesis* **1980**, 318.

The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The resulting oil was recrystallized from hexane–acetone to give 0.49 g (48%) of dimethyl *N*-methyl-2-phenylpyrrole-3,4-dicarboxylate (**8**): mp 117–118 °C; IR (KBr) 2875, 1700, 1650, 1600, 1530, 1440, 1390, 1360, 1300, 1240, 1205, 1180, 1170, 1070, 990, 850, and 780 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.50 (s, 3 H), 3.70 (s, 3 H), 3.85 (s, 3 H), 7.25 (s, 1 H), and 7.38 (s, 5 H); *m/e* 273 (M^+), 244 (base), 243, 212, 184, 159, 128, 115, 105, 91, and 77; UV (methanol) 262 nm (ϵ 10 250).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.76; H, 5.57; N, 5.10.

Reaction of *N*-Methylbenzenecarboximidothioic Acid Methyl Ester (9) with (Trimethylsilyl)methyl Triflate and Dimethyl Acetylenedicarboxylate. To a sample containing 500 mg of *N*-methylthiobenzamide,[52] in 10 mL of tetrahydrofuran was added 3.0 g of methyl iodide. The reaction mixture was stirred at 25 °C for 12 h and the yellow salt which precipitated was collected to give 674 mg (70%) of a solid. This material was treated with a sodium bicarbonate solution. The aqueous layer was extracted with chloroform and the organic extracts were dried over magnesium sulfate. Removal of the solvent under reduced pressure left 340 mg (81%) of an oil which was used in the next step without purification: NMR ($CDCl_3$, 90 MHz) δ 2.07 (s, 3 H), 2.40 (s, 3 H), 3.21 (s, 3 H), 3.50 (s, 3 H), and 7.20–7.56 (m, 5 H).

To a sample containing 340 mg of the above oil in 15 mL of dimethoxyethane was added 505 mg of (trimethylsilyl)methyl triflate. After the solution was stirred at 25 °C for 15 h, 292 mg of dimethyl acetylenedicarboxylate and 320 mg of cesium fluoride were added and stirring was continued for another 10 h. Standard workup gave a 74% yield of dimethyl 1-methyl-2-phenylpyrrole-3,4-dicarborboxylate (**8**).

Reaction of *N*-Methyl-*N*-[(trimethylsilyl)methyl]benzamide (10) with Trimethyloxonium Tetrafluoroborate and Dimethyl Acetylenedicarboxylate. To a 703 mg sample of benzoyl chloride in 10 mL of pyridine was added 636 mg of *N*-methyl-*N*-[(trimethylsilyl)methyl]amine.[53] The mixture was stirred for 12 h, was then acidified with dilute hydrochloric acid, and extracted with chloroform. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure to give 1.18 g (90%) of *N*-methyl-*N*-[(trimethylsilyl)-methyl]benzamide (**10**) as an oil which was used in the next step without further purification: NMR (CCl_4), 90 MHz) δ 0.10 (s, 9 H), 2.91 (s, 3 H), 2.93 (s, 2 H), and 7.30 (s, 5 H).

To 1.18 g of the above compound in 20 mL of dichloromethane was added 950 mg of trimethyloxonium tetrafluoroborate. After the reaction was stirred for 10 h, the solvent was removed under reduced pressure and was replaced by 20 mL of dimethoxyethane. To this solution was added 640 mg of dimethyl acetylenedicarboxylate and 693 mg of cesium fluoride. The mixture was stirred for 12 h at 25 °C, was then washed with water, dried over magnesium sulfate, and concentrated under reduced pressure to give pyrrole **8**, mp 117–118 °C, in 58 % yield.

Preparation of Dimethyl *N*-Benzyl-2-phenylpyrrole-3,4-dicarboxylate (13). To 1.4 g of benzoyl chloride in 20 mL of pyridine was added 1.94 g of *N*-benzyl-*N*-[(trimethylsilyl)-methyl]amine.[53] The mixture was stirred at 25 °C for 12 h and was worked up in the normal fashion to give 1.2 g (42%) of *N*-benzyl-*N*-[(trimethylsilyl)methyl]benzamide (**11**) as an oil which was used in the next step without further purification: NMR ($CDCl_3$, 90 MHz) δ 0.15 (s, 9 H), 2.92 (s, 2 H), 4.55 (bs, 2 H), and 7.08–7.48 (m, 10 H).

To 600 mg of the above amide in 15 mL of methylene chloride was added 500 mg of trimethyloxonium tetrafluoroborate. After the reaction was stirred for 12 h, the solvent was removed under reduced pressure and was replaced by 15 mL of dimethoxyethane. To this solution was added 284 mg of dimethyl acetylenedicarboxylate and 300 mg of cesium fluoride. The mixture was stirred at 25 °C for 12 h, was then washed with water, dried over magnesium sulfate, and concentrated under reduced pressure to give 440 mg (74%) of dimethyl *N*-benzyl-2-phenylpyrrole-3,4-dicarboxylate (**13**) as a crystalline solid: mp 95–96 °C; IR (KBr) 3000, 2875, 1715, 1685, 1525, 1495, 1445, 1385, 1305, 1245, 1205, 1185, 1155, 1075, 865, 775, 755, and 705 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.72 (s, 3 H), 3.89 (s, 3 H), 4.91 (s, 2 H), 7.23 (s, 1 H), and 6.83–7.44 (m, 10 H); *m/e* 349 (M^+), 318, 216, 184, 159, 149, 128, 110, 91 (base), and 77; UV (methanol) 260 nm (ϵ 10 500).

Anal. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01. Found: C, 72.03; H, 5.48; N, 3.96.

Reaction of *N*-Benzyl-*N*-[(trimethylsilyl)methyl]benzamide (11) with Methyl Trifluoromethanesulfonate and Methyl Propiolate. A solution containing 1.5 g of **11** in 10 mL of dimethoxyethane was treated with 820 mg of methyl trifluoromethanesulfonate at 25 °C for 2 h and subsequently with 760 mg of cesium fluoride and 430 mg of methyl propiolate. After stirring at 25 °C for 12 h, the mixture was washed with 10 mL of a 10% sodium hydroxide solution and was taken up in 10 mL of chloroform. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column with a 5% ether–hexane mixture as the eluent. The major isomer contained 450 mg (32%) of a white solid, mp 113–114 °C, whose structure was assigned as methyl *N*-benzyl-2-phenylpyrrole-3-carboxylate (**14**) on the basis of its spectral properties: IR (KBr) 3080, 3040, 2960, 1710, 1550, 1490, 1440, 1385, 1255, 1095, 1020, 930, 770, 735, and 70 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.68 (s, 3 H), 4.94 (s, 2 H), 6.68 (d, 1 H, J = 3.2 Hz), 6.95 (d, 1 H, J = 3.2 Hz), 7.18–7.40 (m, 10 H); UV (methanol) 265 nm (ϵ 11 0–00); *m/e* 291 (M^+), 149, 97, and 91.

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.32; H, 5.88; N, 4.81. Found: C, 78.07; H, 5.93; N, 4.76.

The minor cycloadduct isolated from the column contained 225 mg (16%) of a pale yellow oil whose structure was assigned as methyl *N*-benzyl-2-phenylpyrrole-4-carboxylate (**15**) on the basis of its spectral properties: IR (neat) 3080, 3040, 2960, 1710, 1620, 1565, 1520, 1480, 1450, 1385, 1255, 1215, 1100, 1005, 935, 835, 760, 730, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.78 (s, 3 H), 5.08 (s, 2 H), 6.63 (d, 1 H, J = 1.9 Hz), 6.92 (d, 1 H, J = 1.9 Hz), and 7.14–7.30 (m, 10 H); UV (methanol) 265 (ϵ 16 300); *m/e* 291 (M^+), 141, 105, 91 (base), and 77.

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.32; H, 5.88; N, 4.81. Found: C, 78.16; H, 5.80; N, 4.75.

Preparation of Methyl *N*-Benzyl-2-phenyl-4,5-dihydropyrrole-3-carboxylate (16). A solution containing 1.0 g of **11** in 10 mL of dimethoxyethane was treated with 550 mg of methyl trifluoromethanesulfonate at 25 °C for 2 h and then with 510 mg of cesium fluoride and 300 mg of methyl acrylate. After stirring for 12 h the reaction mixture was washed with a 10% sodium hydroxide solution and taken up in 10 mL of chloroform. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column with a 5% ether–hexane mixture as the eluent to give 390 mg (39%) of a white solid, mp 101–102 °C, whose structure was assigned as methyl *N*-benzyl-2-phenyl-4,5-dihydropyrrole-3-carboxylate: IR (KBr) 3040, 2950, 2860, 1690, 1610, 1570, 1495, 1450, 1350, 1210, 1170, 1100, 890, 765, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) 2.60–2.87 (m, 2 H), 3.16–3.40 (m, 2 H), 3.34 (s, 3 H), 3.86 (s, 2 H), 6.92–7.28 (m, 10 H); UV (methanol) 317 (ϵ 15 000) and 265 nm (ϵ 8700); *m/e* 293 (M^+), 291, 167, 149 (based), 97, and 91.

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.78; H, 6.53; N, 4.77. Found: C, 77.67; H, 6.55; N, 4.72.

Oxidation of a sample of **16** with DDQ produced pyrrole **14** as the only product.

Reaction of *N*-Methylbenzenecarboximidothioic Acid Methyl Ester (9) with (Trimethylsilyl)methyl Triflate and Methyl Propiolate. To a sample containing 825 mg of **9** in 15 mL of dimethoxyethane was added 1.2 g of (trimethylsilyl)methyl triflate. After the reaction was stirred at 25 °C for 2 h, 850 mg of methyl propiolate and 750 mg of cesium fluoride was added. The mixture was stirred for 10 h and was then worked up in the normal fashion. Chromatography of the crude residue on silica gel with a 5% ether–hexane mixture as the eluent produced a mixture of two pyrroles. The first pyrrole to be eluted from the column contained 444 mg (43%) of a white solid, mp 91–92°C, whose structure is assigned as methyl *N*-methyl-2-phenylpyrrole-3-carboxylate (**18**): IR (KBr) 3060, 2960, 1700, 1550, 1495, 1440, 1415, 1350, 1275, 1210, 1165, 1060, 1030, 1015, 930, 915, 790, 765, 740, and 700 cm^{-1}; NMR ($CDCl_3$), 90 MHz) δ 3.43 (s, 3 H),

(52) Voss, J.; Walter, W. *Liebigs Ann. Chem.* **1968**, *209*, 716.
(53) Duff, J. M.; Brook, A. G. *Can. J. Chem.* **1977**, *55*, 2589.

3.62 (s, 3 H), 6.59 (ABq, 2 H, J = 3.2 Hz), and 7.38 (s, 5 H); UV (methanol) 272 nm (ϵ 9800); m/e 215 (M^+), 184, 149, 97, and 95.

Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.33; H, 6.16; N, 6.44.

The second material isolated from the column contained 447 mg (43%) of a pale yellow oil whose structures was assigned as methyl N-methyl-2-phenylpyrrole-4-carboxylate (**19**): IR (neat) 3070, 3040, 2955, 1710, 1610, 1565, 1550, 1450, 1380, 1250, 1220, 1100, 1000, 760, and 70 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.60 (s, 3 H), 3.78 (s, 3 H), 6.58 (d, 1 H, J = 1.9 Hz), 7.28 (d, 1 H, J = 1.9 hz), and 7.32 (m, 5 H); UV (methanol) 264 nm (ϵ 14 500); m/e 215 (M^+), 184, 149 (base), 115, 105, and 77.

Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.48; H, 6.11; N, 6.50.

Preparation of Dimethyl N-Benzyl-2-[2-phenyl-2-(methylthio)ethenyl]-2,5-dihydropyrrole-3,4-dicarboxylate (23). To a sample containing 500 mg of 3-(dimethylamino)thiocrotonophenone[54] in 20 mL of tetrahydrofuran was added 3.0 mL of methyl iodide and the mixture was stirred for 3 h at 25 °C. The resulting precipitate was filtered to give 670 mg (81%) of a yellow salt which was suspended in 20 mL of benzene. To this mixture was added 203 mg of benzylamine and the solution was stirred at 25 °C for 1 h. The mixture was filtered and the solvent was concentrated under reduced pressure. The residue was taken up in 20 mL of dimethoxyethane. To this solution was added 472 mg of (trimethylsilyl)methyl triflate. After the reaction was stirred for 5 h at room temperature, 284 mg of dimethyl acetylenedicarboxylate and 304 mg of cesium fluoroborate were added. The mixture was stirred for 12 h at 25 °C and was washed with sodium bicarbonate. The solvent was dried over magnesium sulfate and concentrated under reduced pressure to give a yellow oil. This material was subjected to silica gel chromatography to give 302 mg (36%) of dihydropyrrole **23** whose structure was assigned on the basis of its spectral properties: IR (neat) 2900, 2870, 2790, 1720, 1695, 1650, 1590, 1580, 1480, 1430, 1350, 1310, 1270, 1150, 1070, 1020, 960, 910, 850, 820, 760, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.21 (s, 3 H), 3.28 (d, 1 H, J = 15.0 Hz), 3.35 (dd, 1 H, J = 15.7 and 4.5 Hz), 3.71 (s, 3 H), 3.80 (dd, 1 H, J = 15.7 and 4.5 Hz), 3.85 (s, 3 H), 3.90 (d, 1 H, J = 15.0 Hz), 4.56 (m, 1 H), 5.38 (d, 1 H, J = 9.3 Hz), 7.14–7.25 (m, 10 H); UV (methanol) 277 nm (ϵ 6500); m/e 423, 376, 374, 344, 332 (base), 300, 286, 218, 186, 150, and 91.

The structure of **23** was further supported by an oxidation to the corresponding pyrrole. A 660-mg sample of **23** in 20 mL of benzene was stirred in the presence of 700 mg of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone at 25 °C for 10 h. The dark black reaction mixture was washed with a sodium carbonate solution followed by water and was then dried over magnesium sulfate to give 410 mg (65%) of dimethyl N-benzyl-2-[2-phenyl-2-(methylthio)ethenyl]pyrrol-3,4-dicarboxylate (**24**) as a crystalline solid: mp 103–104 °C; IR (KBr) 2850, 1680, 1650, 1580, 1520, 1480, 1430, 1410, 1380, 1270, 1235, 1180, 1135, 1055, 975, 940, 800, and 740 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.18 (s, 3 H), 3.69 (s, 3 H), 3.70 (s, 3 H), 4.55 (s, 2 H), 6.12 (s, 1 H), 6.98 (s, 1 H), and 7.21 (m, 10 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 15.89, 51.19, 51.42, 110,59, 115.24, 115.42, 126.94, 127.36, 128.03, 128.49, 128.65, 128.78, 134.12, 136.03, 137.45, 146.04, 163.95, and 165.06; m/e 421 (M^+), 326, 325, 324 (base), 207, 167, and 166; UV (methanol) 303 nm (ϵ 9500).

Anal. Calcd for $C_{24}H_{23}NO_4S$: C, 68.33; H, 5.46; N, 3.32. Found: C, 68.19; H, 5.50; N, 3.29.

Preparation of N-Benzyl-2-methoxy-5-(m-nitrophenyl)-2-phenyloxazolidine (25). A solution containing 1.5 g of N-benzyl-N-[(trimethylsilyl)methyl]benzamide (**11**) in 10 mL of dimethoxyethane was treated with 820 mg of methyl trifluoromethanesulfonate at 25 °C for 2 h and subsequently with 760 mg of cesium fluoride and 480 mg of m-nitrobenzaldehyde. After stirring at 25 °C for 12 h the mixture was rapidly washed with a 10% sodium hydroxide solution and was taken up in chloroform. The organic layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The crude residue was chromatographed on a thick-layer plate with ether–hexane as the eluent. The major component obtained was a light yellow oil (64%) whose structure was assigned as oxazolidine **25** on the basis of its spectral data and by its hydrolysis to methyl benzoate: IR (neat) 3180, 2940, 2860, 2800, 1730, 1610, 1535, 1460, 1360, 1270, 1180, 1120, 1030, 810, and 720 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.43 (s, 3 H), 2.80 (dd, 1 H, J = 15.0 and 6.7 Hz), 3.05 (dd, 1 H, J = 15.0 and 6.7 Hz), 3.61 (s, 2 H), 6.21 (t, 1 H, J = 6.7 Hz), and 7.08–8.30 (m, 14 H); UV (methanol) 228 (ϵ 16 300) and 263 nm (ϵ 10 700); m/e 149, 134 (base), 105, and 91.

Anal. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18. Found: C, 70.49; H, 5.85; N, 6.94.

Preparation of N-(3-Methoxy-2-cyclohexen-1-ylidene)benzenemethanamine (27). A mixture containing 890 mg of 3-(benzylamine)-2-cyclohexen-1-one[55] (**26**) in 4 mL of methyl iodide was heated at reflux for 12 h. At the end of this time the excess methyl iodide was removed under reduced pressure and the resulting residue was triturated with tetrahydrofuran to give 1.14 g (75%) of a white solid, mp 137–138 °C, which corresponds to the hydroiodide salt of **27**: IR (KBr) 3100–2400 (broad), 1605, 1550, 1440, 1320, 1200, 1160, 1090, 1045, 975, 905, 850, 765, and 705 cm^{-1}; NMR (Me_2SO-d_6, 90 MHz) δ 1.98 (quintet, 2 H, J = 6.0 Hz), 2.55 (t, 2 H, J = 6.0 Hz), 3.25 (t, 2 H, J = 6.0 Hz), 4.02 (s, 3 H), 4.91 (s, 2 H), 5.90 (s, 1 H), and 7.2–7.7 (m, 5 H).

Anal. Calcd for $C_{14}H_{18}NOI$: C, 48.99; H, 5.29; N, 4.08; I, 36.98. Found: C, 48.87; H, 5.31; N, 4.07; I, 37.08.

A 900-mg sample of the above salt in 10 mL of ether was stirred with 5 mL of a 5% sodium hydroxide solution for 30 min. The organic layer was separated, dried over magnesium sulfate, and concentrated under reduced pressure to give N-(3-methoxy-2-cyclohexen-1-ylidene)benzenemethanamine (**27**) as a clear oil:[56] NMR ($CDCl_3$, 90 MHz) δ 1.7–2.0 (m, 2 H), 2.15–2.60 (m, 4 H), 3.65 (s, 3 H), 4.55 (s, 2 H), 5.61 (s, 1 H), and 7.15–7.45 (m, 5 H). This material was used in the next step without further purification.

General Procedure for the Generation and Cycloaddition Reactions of the Azomethine Ylide Derived from N-(3-Methoxy-2-cyclohexen-1-ylidene)benzenemethanamine (27). To a stirred solution containing 0.6 mmol of **27** in 8 mL of dry dimethoxyethane was added 0.66 mmol of (trimethylsilyl)methyl triflate. The resulting mixture was stirred at 25 °C for 20 min, then 0.66 mmol of the appropriate dipolarophile and 0.66 mmol of cesium fluoride were added, and the mixture was allowed to stir at 25 °C for 12 h. At the end of this time the solution was poured into a saturated sodium chloride solution and extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The resulting residue was purified by silica gel chromatography with a 5% ether–hexane mixture as the eluent. In this manner the following compounds were prepared.

Methyl 1-Benzyl-7-methoxy-1-azaspiro[4.5]deca-3,6-diene-4-carboxylate (29). A yield of 70% of **29** was obtained: IR (neat) 3050, 3030, 2940, 2830, 2790, 1725, 1660, 1495, 1455, 1440, 1380, 1360, 1320, 1270, 1220, 1190, 1130, 1080, 1045, 1020, 1000, 980, 925, 900, 880, 840, 820, 795, and 705 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.60–2.27 (m, 6 H), 3.31 (dd, 1 H, J = 18.0 and 2.5 Hz), 3.54 (dd, 1 H, J = 18.0 and 2.5 Hz), 3.60 (s, 3 H), 3.73 (s, 3 H), 3.68 (d, 1 H, J = 17.0 Hz), 3.88 (d, 1 H, J = 17.0 Hz), 4.51 (s, 1 H), 6.76 (t, 1 H, J = 2.5 Hz), and 7.13–7.45 (m, 5 H); C^{13} NMR ($CDCl_3$, 20 MHz) δ 20.1 (t), 27.3 (t), 31.7 (t), 51.2 (g), 54.06 (g), 54.14 (t), 56.3 (t), 69.1 (s), 95.8 (d), 126.7 (d), 128.3 (d), 139.1 (d), 140.6 (s), 141.5 (s), 159.5 (s), and 164.1 (s).

Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.64; H, 7.29; N, 4.42.

Methyl 1-Benzyl-7-methoxy-1-azaspiro[4.5]dec-6-ene-4-carboxylate (30). A yield of 85% of **30** was obtained: IR (neat) 3010, 2930, 2830, 2790, 1725, 1660, 1605, 1490, 1450, 1430, 1380, 1360, 1260, 1220, 1170, 1080, 1030, 1020, 980, 950, 840, 745, and 705 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.3–2.35 (m, 8 H), 2.50–3.0 (m, 3 H), two sets of methyl singlets for both diastereomers (1.4:1 ratio) at 3.51, 3.59, 3.65, and 3.67 (6 H), 3.30–3.85 (m, 2 H), 4.45 (s, 1 H), and 7.10–7.45 (m, 5 H); m/e 315 (M^+), 256, 214, 138, 121, 91 (base), 65, and 55.

Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.20; H, 8.01; N, 4.39.

(54) Lin, Y.; Lang, S. A. *J. Org. Chem.* **1980**, *45*, 4857.

(55) Jirkovsky, I. *Can. J. Chem.* **1974**, *25*, 55.

(56) Greenhill, J. V. *J. Chem. Soc. B* **1969**, 299.

Acid Hydrolysis of Methyl 1-Benzyl-7-methoxy-1-azaspiro[4.5]dec-6-ene-4-carboxylate (30). To a solution containing 115 mg of **30** in 2 mL of acetone was added 0.6 mL of a 1.0 N aqueous hydrochloric acid solution. The mixture was stirred for 1 h at 25 °C and was then concentrated under reduced pressure. The residue was extracted with methylene chloride and the aqueous solution was made basic with a 10% sodium hydroxide solution. The mixture was extracted with methylene chloride and the organic extracts were dried over magnesium sulfate. Removal of the solvent under reduced pressure left 90 mg (90%) of a colorless oil whose structure was identified as 1-benzyl-3-(3-oxo-1-cyclohexen-1-yl)-2-pyrrolidinone (**32**): IR (neat) 3010, 2930, 2860, 1670 (broad), 1625, 1490, 1430, 1360, 1350, 1330, 1260, 1200, 1090, 1035, 970, 930, 900, 740, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.8–2.25 (m, 4 H), 2.25–2.50 (m, 4 H), 3.2–3.45 (m, 3 H), 4.51 (s, 2 H), 6.02 (s, 1 H), and 7.15–7.45 (m, 5 H); *m/e* 269 (M^+), 268, 105, 91 (base), 65, and 55.

Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.63; H, 7.09; N, 5.13.

The structure of **32** was further verified by comparison with an independently synthesized sample. To a solution of LDA prepared from 3 mL of a 1.26 M *n*-butyllithium solution and 0.7 mL of diisopropylamine in 5 mL of tetrahydrofuran was added 438 mg of *N*-benzylpyrrolidin-2-one in 2 mL of tetrahydrofuran. After the solution was stirred at −78 °C for 30 min, a mixture containing 350 mg of 3-ethoxycyclohex-2-enone[57] in 1.5 mL of tetrahydrofuran was added and the solution was allowed to warm to room temperature over a 2-h period. The mixture was quenched with a saturated ammonium chloride solution and was then acidified with a 3 N hydrochloric acid solution. The mixture was extracted with ether and the ethereal extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting clear oil contained 530 mg of **32** which is identical in every detail with a sample obtained from the acid hydrolysis of **30**.

Preparation of 3-(Benzylamino)-2-cyclohexene-1-thione. To a sample containing 2.01 g of 3-(benzylamino)-2-cyclohexen-1-one in 100 mL of dimethoxyethane was added 2.43 g of Lawesson's reagent[58] at 0 °C. After stirring for 15 min the mixture was poured into 100 mL of water and was then extracted with chloroform. The organic extracts were dried over magnesium sulfate and concentrated under reduced pressure. The resulting residue was passed through a silica gel column with chloroform as the eluent to give 1.84 g (85%) of 3-(benzylamino)-2-cyclohexene-1-thione as a crystalline solid:[59] mp 146–147 °C; IR (KBr) 3170, 3010, 2940, 1530, 1440, 1400, 1355, 1270, 1240, 1210, 1150, 1080, 1020, 900, 840, 750, and 705 cm^{-1}; UV (95% ethanol) 380 (ϵ 19 300) and 288 nm (ϵ 19 100); NMR ($CDCl_3$, 90 MHz) δ 1.81 (quintet, 2 H, J = 6.0 Hz), 2.40 (t, 2 H, J = 6.0 Hz), 2.75 (t, 2 H, J = 6.0 Hz), 4.32 (d, 2 H, J = 6.0 Hz), 6.45 (s, 1 H), 6.85 (bs, 1 H), and 7.1–7.4 (m, 5 H); *m/e* 217 (M^+), 167, 149, 91 (base), and 71.

Anal. Calcd for $C_{13}H_{15}NS$: C, 71.85; H, 6.96; N, 6.44; S, 14.75. Found: C, 71.72; H, 7.00; N, 6.44; S, 14.80.

General Procedure for the Generation and Cycloaddition Reactions of the Azomethine Ylide Derived from *N*-[3-(Methylthio)-2-cyclohexen-1-ylidene]benzenemethanamine. To a solution containing 365 mg of the above compound in 15 mL of tetrahydrofuran was added 2 mL of methyl iodide and the mixture was allowed to stir at 25 °C for 45 min. The solution was poured into 5 mL of a 10% sodium hydroxide solution and the organic layer was separated, washed with a saturated sodium chloride solution, and dried over magnesium sulfate. The solvent was removed under reduced pressure to give 371 mg (98%) of *N*-[3-(thiomethyl)-2-cyclohexen-1-ylidene]benzenemethanamine as a clear oil: NMR ($CDCl_3$, 90 MHz) δ 1.65–2.0 (m, 2 H), 2.25 (s, 3 H), 2.1–2.55 (m, 4 H), 4.55 (s, 2 H), 6.10 (s, 1 H), and 7.10–7.40 (m, 5 H). This material was used in the next step without any further purification. The cycloaddition procedure used with this compound is the same as that described with **28**. In this manner the following compounds were obtained.

(57) Frank, R. L.; Hall, H. K. *J. Am. Chem. Soc.* **1950**, *72*, 1645.
(58) Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S. O. *Bull. Chim. Belg.* **1978**, *87*, 223.
(59) Walter, W.; Proll, T. *Synthesis* **1979**, 941.

Dimethyl 1-Benzyl-7-(methylthio)-1-azaspiro[4.5]deca-3,6-diene-3,4-dicarboxylate (35). A yield of 80% of **35** was obtained as a clear oil: IR (neat) 3040, 2950, 2850, 2800, 1740, 1730, 1660, 1620, 1580, 1490, 1440, 1370, 1280, 1220, 1155, 1120, 1060, 1040, 970, 920, 855, 835, 805, 745, and 710 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.5–2.35 (m, 6 H), 2.28 (s, 3 H), 3.53 (d, 1 H, J = 12.0 Hz), 3.61 (d, 1 H, J = 12.0 Hz), 3.70 (s, 3 H), 3.80 (s, 3 H), 3.8 (m, 2 H), 5.22 (s, 1 H), and 7.17–7.45 (m, 5 H).

Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.10; H, 6.50; N, 3.62. Found: C, 65.02; H, 6.34; N, 3.68.

Methyl 1-Benzyl-7-(methylthio)-1-azaspiro[4.5]deca-3,6-diene-4-carboxylate (36). A yield of 70% of **36** was obtained as a clear oil: IR (neat) 3060, 3030, 2940, 2870, 2800, 1720, 1605, 1590, 1495, 1460, 1440, 1360, 1320, 1240, 1135, 1080, 1050, 980, 900, 855, 840, 800, 755, and 710 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.5–2.3 (m, 6 H), 2.25 (s, 3 H), 3.38 (dd, 1 H, J = 18.0 and 2.8 Hz), 3.53 (dd, 1 H, J = 18.0 and 2.8 Hz), 3.70 (s, 3 H), 3.71 and 3.84 (d, 1 H, J = 13.0 Hz), 5.17 (s, 1 H), 6.82 (t, 1 H, J = 2.8 Hz), and 7.18–7.50 (m, 5 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 14.24 (q), 20.8 (t), 29.3 (t), 31.5 (t), 51.3 (t), 53.9 (t), 56.3 (q), 68.9 (s), 118.8 (d), 126.8 (d), 128.3 (d), 128.4 (d), 139.3 (s), 139.7 (d), 140.2 (s), 140.8 (s), and 163.8 (s).

Anal. Calcd for $C_{19}H_{23}NO_2S$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.35; H, 7.02; N, 4.06.

Methyl 1-Benzyl-7-(methylthio)-1-azaspiro[4.5]dec-6-ene-4-carboxylate (37). A yield of 68% of **37** was obtained as a clear oil: IR (neat) 3000, 2930, 2780, 1735, 1625, 1600, 1490, 1450, 1440, 1360, 1250, 1170 (broad), 1080, 1040, 1020, 990, 950, 925, 905, 860, 750, and 705 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.40–2.30 (m, 8 H), the NMR shows a 3:1 mixture of two diastereomers with signals at 2.20 (s, 3 H) and 2.27 (s, 3 H), 2.57–2.79 (m, 1 H), 2.80–3.00 (m, 2 H), 3.35 (d, 1 H, J = 13.0 Hz), 3.52 (d, 1 H, J = 13.0 Hz), 3.60 (d, 1 H, J = 13.0 Hz), 3.72 (d, 1 H, J = 13.0 Hz), 3.61 (s, 3 H), 3.66 (s, 3 H), 5.13 (s, 1 H), 5.26 (s, 1 H), and 7.10–7.50 (m, 5 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 14.02, 14.27, 20.80, 21.13, 23.78, 24.75, 25.77, 29.68, 31.88, 48.67, 49.65, 51.31, 51.54, 53.02, 53.26, 54.24, 55.32, 66.48, 66.88, 118.8, 122.7, 126.6, 126.8, 128.1, 129.3, 138.9, 139.2, 140.5, 140.8, 173.4, and 174.2; UV (95% ethanol) 226 nm (ϵ 22 000); *m/e* 313 (M^+, base), 317, 316, 288, 285, 284, 256, 245, 240, 231, 230, 196, 156, 155, 106, 105, 92, and 91.

Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60; N, 4.22; S, 9.66. Found: C, 68.67; H, 7.63; N, 4.19; S, 9.70.

Picrate derivative, mp 143–144 °C.

Anal. Calcd for $C_{25}H_{28}N_4O_9S$: C, 53.56; H, 5.03; N, 9.99; S, 5.72. Found: C, 53.62; H, 5.05; N, 9.96; S, 5.77.

Dimethyl 1-Benzyl-7-(methylthio)-1-azaspiro[4.5]dec-6-ene-*trans*-3,4-dicarboxylate (38). Two diastereomers were obtained which could be separated by thick-layer chromatography on silica gel. The major isomer was formed in 56% yield as a colorless oil: IR (neat) 3020, 2950, 2810, 1730, 1625, 1490, 1440, 1320, 1260, 1200 (broad), 1180, 1130, 860, 820, 750, and 710 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.70–2.0 (m, 4 H), 2.1–2.25 (m, 2 H), 2.20 (s, 3 H), 2.87 (dd, 1 H, J = 9.3 and 7.5 Hz), 3.11 (dd, 12 H, J = 9.3 and 9.0 Hz), 3.29 (d, 1 H, J = 6.8 Hz), 3.55 (ddd, 1 H, J = 9.0, 7.5, and 6.8 Hz), 3.64 (s, 3 H), 3.65 (s, 3 H), 3.51 (d, 1 H, J = 13.8 Hz), 3.59 (d, 1 H, J = 13.8 Hz), 5.05 (s, 1 H), and 7.2–7.4 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.06 (q), 20.5 (t), 29.7 (t), 31.1 (t), 44.2 (q), 51.7 (d), 51.9 (d), 52.1 (t), 52.5 (t), 58.3 (q), 67.4 (s), 118.8 (d), 126.8 (d), 128.1 (d), 128.3 (d), 140.2 (s), 140.3 (s), 172.7 (s), 173.9 (s); UV (95% ethanol) 230 nm (ϵ 19 000); *m/e* 389 (M^+), 375, 374, 342, 314, 282, 254, 245, 230, 192, 177, 154, 151, 135, 105, 91, and 77.

Anal. Calcd for $C_{21}H_{27}NO_4S$: C, 64.76; H, 6.99; N, 3.60; S, 8.23. Found: C, 64.60; H, 7.03; N, 3.60; S, 8.16.

The minor diastereomer was obtained in 31% yield as a colorless oil: IR (neat) 3020, 2950, 2830, 1730, 1630, 1605, 1490, 1440, 1370, 1330, 1200 (broad), 1080, 1040, 985, 950, 860, 840, 820, 750, and 710 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.35–1.47 (m, 1 H), 1.61–1.82 (m, 3 H), 1.98–2.17 (m, 2 H), 2.27 (s, 3 H), 2.87 (t, 1 H, J = 9.5 Hz), 3.01 (dd, 1 H, J = 9.5 and 5.5 Hz), 3.19 (d, 1 H, J = 9.8 Hz), 3.57 (m, 1 H), 3.33 (d, 1 H, J = 13.4 Hz), 3.76 (d, 1 H, J = 13.4 Hz), 3.63 (s, 3 H), 3.69 (s, 3 H), 5.12 (s, 7 H), and 7.3–7.6 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.24 (q), 20.9 (t), 24.0 (t), 29.5 (t), 43.1 (q), 51.2 (t), 51.9 (d), 52.1 (d), 52.9 (t), 57.2 (q), 66.8 (s), 121.5 (d), 126.8 (d), 128.1 (d), 128.3 (d), 139.4 (s),

140.3 (s), 172.3 (s), and 174.1 (s); and 174.1 (s); UV (95% ethanol) 230 nm (ε 14000); *m/e* 389 (M^+), 374, 343, 342, 314, 298, 254, 245, 230, 155, 154 (base), and 91.

Anal. Calcd for $C_{21}H_{27}NO_4S$: C, 64.76; H, 6.99; N, 3.60; S, 8.23. Found: C, 64.57; H, 7.04; N, 3.59; S, 8.15.

Dimethyl 1-Benzyl-7-(methylthio)-1-azaspiro[4.5]dec-6-ene-*cis*-3,4-dicarboxylate (39). A yield of 75% of 39 was obtained as a clear oil: IR (neat) 3010, 2950, 2830, 1730 (broad), 1620, 1600, 1490, 1435, 1360, 1200 (broad), 1090, 1035, 860, 840, 820, 745, and 705 cm^{-1}. Compound **39** consisted of a 1:1 mixture of two diastereomers which could not be separated by silica gel chromatography NMR ($CDCl_3$, 360 MHz) δ 1.65–1.92 (m, 4 H), 2.05–2.27 (m, 2 H), 2.19 (s, 3 H), 2.25 (s, 3 H), 2.91–2.97 (m, 1 H), 3.2–3.38 (m, 2 H), 3.45–3.75 (m, 3 H), 3.61 (s, 3 H), 3.62 (s, 3 H), 3.63 (s, 3 H) and 3.68 (s, 3 H), 5.15 (s, 1 H), 5.22 (s, 1 H), and 7.1–7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (q), 14.2 (q), 21.0 (t), 21.3 (t), 28.5 (t), 29.9 (t), 30.0 (t), 34.3 (t), 42.9 (q), 44.0 (q), 51.3 (d), 51.8 (t), 51.9 (d), 52.3 (t), 52.9 (t), 53.0 (t), 56.98 (q), 57.7 (q), 67.2 (s), 67.8 (s), 119.0 (d), 121.0 (d), 126.8 (d), 127.8 (d), 127.9 (d), 128.0 (d), 139.5 (s), 140.8 (s), 171.9 (s), 172.1 (s), 172.2 (s), and 173.0 (s); UV (95% ethanol) 227 nm (ε 23000); *m/e* 389 (M^+), 374, 342, 314, 254, 245, 230, 198, 154, and 91 (base).

Anal. Calcd for $C_{21}H_{27}NO_4S$: C, 64.76; H, 6.99; N, 3.60; S, 8.23. Found: C, 64.59; H, 6.99; N, 3.56; S, 8.17.

Picrate derivative, mp 160–161 °C.

Anal. Calcd for $C_{27}H_{30}N_4O_{11}S$: C, 52.22; H, 4.88; N, 9.04; S, 5.17. Found: C, 52.35; H, 4.90; N, 8.98, S, 5.20.

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Registry No. **3**, 1775-60-6; **6**, 88329-71-9; **8**, 19611-52-0; **9**, 40780-82-3; **10**, 91003-35-9; **11**, 91003-36-0; **13**, 51220-12-3; **14**, 77643-63-1; **15**, 77643-67-5; **16**, 91003-37-1; **18**, 91003-38-2; **19**, 91003-39-3; **21**, 88329-72-0; **23**, 88329-73-1; **24**, 91003-40-6; **25**, 91003-41-7; **26**, 41609-04-5; **26** (thione), 70134-00-8; **27**, 88329-74-2; **27**·HI, 91003-55-3; **27** (methylthio deriv), 91003-57-5; **28**·TfO^-, 91003-56-4; **29**, 91003-42-8; *cis*-**30**, 91003-43-9; *trans*-**30**, 91003-44-0; **32**, 88329-77-5; **35**, 91003-45-1; **36**, 91003-46-2; **37**, 91003-47-3; **37**·picrate, 91003-58-6; **38** (isomer 1), 91003-48-4; **38** (isomer 2), 91108-47-3; **39** (isomer 1), 91108-48-4; **39** (isomer 2), 91108-49-5; **39**·picrate (isomer 1), 91176-60-2; **39**·picrate (isomer 2), 91176-59-9; **40**, 91003-49-5; **41**, 91003-50-8; **44**, 91003-51-9; **47**, 19012-02-3; **48**, 88636-52-6; **51**, 91003-52-0; **52**, 91003-53-1; $Me_3SiCH_2OSO_2CF_3$, 64035-64-9; CsF, 13400-13-0; (*E*)-$CH_3O_2CCH{=}CHCO_2CH_3$, 624-49-7; $PhCONHCH_3$, 613-93-4; $CH_3O_2CC{\equiv}CCO_2CH_3$, 762-42-5; $PhCSNHCH_3$, 5310-14-5; PhCOCl, 98-88-4; $CH_3NHCH_2SiMe_3$, 18135-05-2; $PhCH_2NHCH_2SiMe_3$, 53215-95-5; $CH_3OSO_2CF_3$, 333-27-7; $HC{\equiv}CCO_2CH_3$, 922-67-8; $CH_2{=}CHCO_2CH_3$, 96-33-3; $PhCSCH{=}CHN(CH_3)_2$, 24301-15-3; $PhC(SCH_3){=}CHCH{=}N(CH_3)_2^+ I^-$, 91003-54-2; $PhCH_2NH_2$, 100-46-9; $CsBF_4$, 18909-69-8; $Br(CH_2)_2CH{=}CH_2$, 5162-44-7; $(CH_3)_3SiCH_2Cl$, 2344-80-1; $(CH_3)_3SiCH_2I$, 4206-67-1; *n*-nitrobenzaldehyde, 99-61-6; *N*-benzylpyrrolidin-2-one, 5291-77-0; 3-ethoxycyclohex-2-enone, 5323-87-5; 2-(3-butenyl)cyclohexane-1,3-dione, 56459-16-6; 2-(3-butenyl)-3-(benzylamino)-2-cyclohexen-1-one, 91003-59-7; 2-(3-butenyl)-3-(benzylamino)-2-cyclohexene-1-thione, 91003-60-0; 3-acetylindole, 703-80-0; 3-indolylacetonitrile, 771-51-7; 3-(1-pyrrolidinylmethylene)-3*H*-indole, 75629-45-7.

Supplementary Material Available: Experimental details are given for the preparation and attempted cycloaddition reactions of 2-(3-butenyl)-*N*-(3-(methylthio)-2-cyclohex-1-ylidene)benzenemethanamine, 6-(3-butenyl)-*N*-(3-methoxy-2-cyclohex-1-ylidene)benzenemethanamine, *N*-[(trimethylsilyl)methyl]-3-acetylindole, [3-[*N*-(trimethylsilyl)methyl]indolyl]-acetonitrile, and *N*-[(trimethylsilyl)methyl]-3-[(α-cyano-α-pyrrolidinyl)methyl]indole (4 pages). Ordering information is given on any current masthead page.

Reaction of *N*-Nitroso- and *N*-Nitro-*N*-alkylamides with Amines

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Several *N*-nitroso- and *N*-nitrocarboxamides have been characterized by ^1H and ^{13}C NMR spectroscopy. These compounds react with ammonia and aliphatic amines to afford mainly carboxamides of general formula $RCONH_2$, RCONHR′, or RCONR′R″. *N*-Nitrosocarboxamides and aromatic amines give poor yields of RCONHAr; by contrast, *N*-nitrocarboxamides and aromatic amines lead to RCONHAr in good yields. The higher thermal stability of the *N*-nitroamides as compared to *N*-nitrosoamides is advantageous in this connection; nevertheless, the principal advantage of the NNO_2 group appears to be that it activates the nucleophilic attack to the carbonyl of the amide function more than the NNO group, as has been demonstrated by competitive experiments. The reaction of *N*-nitroso- and *N*-nitro-*N*-methylsulfonamides with ammonia and diethylamine has been studied as well; whereas *N*-methyl-*N*-nitro-*p*-toluenesulfonamide reacts as *N*-nitrocarboxamides, transnitrosation is predominant with *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide.

That nucleophilic attacks to the rather reluctant amide bonds may be greatly favored by their previous N-nitrosation is well-known.[1] In fact, the most general method of generation of diazo alkanes is based upon the easy reaction of nitrosocarboxamides and nitrososulfonamides with strong bases. N-Nitration, although less investigated, also activates, of course, the electrophilicity of the carbonyl group of the amides, the reaction of *N*-nitrocarboxamides and *N*-nitrocarbamates with hydroxide and alkoxide anions having been employed to prepare *N*-nitroamines.[1] Hydrides also react with certain nitrosoamides under mild conditions to afford alcohols,[2] but the reaction is often complicated by the appearance of several byproducts.[3] With the aim of finding a smooth method

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